R E M A R K S

The Office Action of July 29, 2002 presents the examination of claims 1-6, 21-22, and 25-27. Claim 3 is canceled. Claim 1 is amended. Support for the amendment to claim 1 is found in canceled claim 3. No new matter is inserted into the application.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 1-6 and 21-22 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. Claim 3 is canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection applied to the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Specifically, the Examiner maintains that the phrase "partly but not wholly overlapping" in claim 1 is unclear. The Examiner states that the claim would be more definite if it read "said fragment comprising an IgG epitope and an IgE epitope partly but not completely…." In response to the Examiner's remarks, Applicants amend claim 1 as suggested by the Examiner in order to overcome the rejection.

Applicants respectfully submit that the instant claims fully comply with the requirements of 35 U.S.C. § 112, second paragraph.

Withdrawal of the instant rejection is therefore respectfully requested.

Rejections under 35 U.S.C. §§ 102, 103

Rogers et al.

The Examiner maintains the rejection of claims 1-2, 4, and 6 under 35 U.S.C. § 102(b) for allegedly being anticipated by Rogers et al. (*Mol. Immunol.* 31(13):955-966, 1994). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

First of all, the subject matter of claim 3 is incorporated into claim 1. As claim 3 is not rejected over Rogers et al., the rejection is overcome.

In the Reply filed on May 15, 2002, Applicants argued that Rogers et al. discloses recombinant proteins comprised of peptides containing recombined T cell epitopes, but fails to disclose an IgG epitope on the recombinant proteins, and therefore fails to anticipate the present invention. In response, the Examiner states that the burden is on Applicant to prove that the peptides of Rogers et al. do not contain the IgG epitope. Applicants respectfully disagree.

The Examiner has not shifted the burden to Applicants

It is respectfully submitted that the burden is on the Examiner in the first instance to demonstrate that the prior art inherently possesses the claimed features. "Once a reference teaching product appearing to be substantially identical is made the basis of a rejection, **and the Examiner presents evidence or reasoning tending to show inherency**, the burden shifts to the Applicant to show an unobvious different." U.S. Pat. & Trademark Off., Manual Pat. Examining Proc. § 2112 (8th ed. 2001) (emphasis added). In the instant case, the Examiner has failed to present evidence or reasoning tending to show that the peptides disclosed in Rogers et al. possess an IgG epitope.

In making first making the rejection over Rogers et al. in the Office Action dated January 15, 2002, the Examiner states,

> "Rogers et al. teach recombinant proteins comprised of peptides containing recombined T cell epitopes which exhibit reduced IgE binding (i.e. non-anaphylactic; see the Abstract in particular). Further, Rogers et al. teaches that human T cell epitope maps of important allergens have been defined, including Betv1, (see page 955, column 2). Figure 1 depicts the recombinant polypeptide, Figure 4, depicts IgE binding, and Figure 7 depicts tolerization with the recombinant polypeptide. The approach is applicable to allergen such as Betv1 (see the Discussion in particular). The recombinant polypeptides were injected into mice in PBS (i.e. a carrier; see page 960, left column, middle section).
>
> The prior art teachings anticipate the claimed invention."

Nowhere in this recitation does the Examiner present evidence or reasoning tending to show that the peptides disclosed in Rogers et al. inherently possess the IgG epitope. When Applicants pointed out that Rogers et al. failed to disclose an IgG epitope on the recombined proteins (see Reply filed on May 15, 2002), the Examiner responded,

> "However, Applicant is guided to MPEP section 2112 which discloses that once the office has established that the prior art is substantially similar to the claimed invention, the burden shifts to Applicant to demonstrate the differences. In other words the burden is on Applicant to demonstrate all the peptides disclosed by Rogers to be non-anaphylatic and not contain an IgE epitope[1] do not contain an IgG epitope."

Applicants agree that MPEP § 2112 states that once the Office has established substantial similarity and the Examiner presents evidence or reasoning tending to show inherency, the burden shifts to Applicants to show an unobvious difference. However, the Examiner is missing an essential piece of the rejection. Again, nowhere in the rejections has the Examiner provided evidence or reasoning, either implicit or explicit, tending to show that the peptides disclosed by Rogers et al. inherently possess all of the claimed features of the present invention. "In relying upon a

[1] Applicants do not assert that Rogers et al. fails to disclose an IgE epitope on the recombinant peptides. Applicants assume that the statement "not contain an IgE epitope" is a typographical error.

theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). Again, the Examiner has failed to provide any basis in fact and/or technical reasoning.

For this reason, the Examiner has not met the burden of proof imposed by MPEP § 2112 and the burden has not shifted to Applicants. Therefore, the rejection is technically deficient and, as such, must be withdrawn.

The peptides disclosed in Rogers et al. do not inherently possess an IgG epitope

In the interest of compact prosecution, however, Applicants respectfully submit that the peptides disclosed by Rogers et al. do not inherently possess an IgG epitope. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill in the art. Inherency, however, may not be established by probabilities or possibilities. The mere fact that

a certain thing may result from a given set of circumstances is not sufficient.'" In re Robertson, 169 F.3d 743, 745 (Fed. Cir. 1999) (citations omitted). Thus, in order for the peptides of Rogers et al. to inherently possess an IgG epitope, it must be established that (1) the IgG epitope is necessarily present, and (2) that the presence of the IgG epitope would be recognized by one of ordinary skill in the art.

Regarding the first requirement, there is no evidence of record regarding Rogers et al. showing that the peptides disclosed therein necessarily contain the IgG epitope. The peptides disclosed by Rogers et al. are comprised of three *non-contiguous* T cell reactive regions of less than 30 amino acids in length (see Abstract). The non-contiguous regions were artificially combined into single polypeptide chains, expressed in E. coli, and examined for their ability to bind to human IgE. The IgG epitope and IgE epitopes of the instantly claimed protein allergen partly but not completely overlap. Since the peptides of Rogers et al. are non-contiguous, it is possible that the peptides were digested in a region wherein a theoretical IgG epitope was excised off of the peptide. Thus, even though the peptides *may* contain the IgG epitope, it is likely that they do not contain the IgG epitope. Thus, the missing descriptive matter (i.e., the IgG epitope) is not

necessarily found on the peptides. Since the first requirement of necessity is not met in the instant case, inherency cannot be established. Further, the likelihood or probability that the peptides contain an IgG epitope cannot be determined theoretically. The presence or absence of the IgG epitope can only be proven by experimental tests. These tests were not preformed in the Rogers et al. publication.

Regarding the second requirement, the skilled artisan would not recognize that the peptides of Rogers et al. possess an IgG epitope for the following reasons. IgG only is mentioned once in Rogers et al., on page 958 under the section heading "Assessment of human cat-allergic IgE binding by ELISA." Therein, Rogers et al. states, "This plasma pool had been depleted of most of the IgG antibodies by passage over Protein G-Agarose…." When this "purified" plasma is used together with the peptides, there is no possibility to determine whether or not there is an IgG epitope on the recombinant proteins since there are no IgG molecules left to bind to a possible IgG epitope. The aim of the Rogers et al. study was to determine if the disclosed peptides have IgE binding capability and therefore no effort was given to test a possible IgG binding capability. As such, the skilled artisan would have no means for determining whether or not the peptides possessed an IgG

epitope, and consequentially would not even consider whether or not the peptides possessed an IgG epitope. Since the second requirement of recognition is not met, inherency cannot be established.

For this reason, the rejection of the instant claims over Rogers et al. is improper. Withdrawal of the rejection is therefore respectfully requested.

Rogers et al. in view of USP '783

The Examiner maintains the rejection of claims 3 and 21 under 35 U.S.C. § 103(a) for allegedly being obvious over Rogers et al. in view of U.S. Patent 4,629,783. Claim 3 is canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection applied to the pending claim 21. Reconsideration of the claim and withdrawal of the instant rejection are respectfully requested.

Applicants respectfully submit that the use of a peptide linker is moot since none of the references anticipate or suggest an IgG epitope on the recombinant proteins.

Withdrawal of the rejection is therefore respectfully requested.

Rogers et al. in view of USP '783 and USP '939

The Examiner also maintains the rejection of claim 22 under 35 U.S.C. § 103(a) for allegedly being obvious over Rogers et al. in view of U.S. Patent 4,629,783, and U.S. Patent 6,126,939. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Applicants respectfully submit that the use of a peptide linker is moot since none of the references anticipate or suggest an IgG epitope on the recombinant proteins.

Withdrawal of the rejection is therefore respectfully requested.

Vrtala et al.

The Examiner maintains the rejection of claims 1-2 and 4-5 under 35 U.S.C. § 102(a) for allegedly being anticipated by Vrtala et al. (*J. Clin. Immunol.* 99(7):1674-1681, 1997). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

First of all, the subject matter of claim 3 is incorporated into claim 1. As claim 3 is not rejected over Vrtala et al., the rejection is overcome.

In the Reply of May 15, 2002, Applicants stated that Applicants are in the process of obtaining a Declaration stating that the peptides disclosed in Vrtala et al. do not have an IgG epitope. Upon further consideration, however, Applicants retract this statement and no such Declaration will be forthcoming. Instead, Applicants instead wish to remove the reference as prior art against the present application.

35 U.S.C. § 102(a) states, "A person shall not be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent." As further stated in MPEP § 2132, "The term 'others' means any entity which is different from the inventive entity. The entity need only differ by one person to be 'by others.'" U.S. Pat. & Trademark Off., Manual Pat. Examining Proc. § 2132 (8th ed. 2001).

The inventors of the present application are: VALENTA, VRTALA, VANGELISTA, EICHLER, SPERR, VALENT, EBNER, KRAFT, AND GRÖNLUND. The authors of Vrtala et al. are: VRTALA, HIRTENLEHNER, VANGELISTA, PASTORE, EICHLER, SPERR, VALENT, EBNER, KRAFT, and VALENTA. Thus, the "authorship entity" is different from the "inventive entity" in

that (1) HIRTENLEHNER and PASTORE are authors but not inventors, and (2) GRÖNLUND is an inventor but not an author.

It is well established that Applicant's disclosure of his or her own work within the year before the application filing date cannot be used against him or her under 35 U.S.C. § 102(a). In re Katz, 687 F.2d 450 (CCPA 1982). Applicants have previously submitted a *Katz* Declaration under 35 U.S.C. § 131 [*sic*, § 132] in parent application 08/998,549 (now abandoned) executed by VRTALA, VANGELISTA, EICHLER, SPERR, VALENT, EBNER, KRAFT, and VALENTA, a copy of which is attached hereto. In the Declaration, the declarers stated that they are co-inventors of the present application, and that any disclosure in Vrtala et al. which is not within the scope of the claimed invention was neither conceived nor reduced to practice any HIRTENLEHNER and PASTORE, and that any disclosure in Vrtala et al. which is within the scope of the claimed invention and may have been performed by HIRTENLEHNER or PASTORE, was done under the supervision of one or more of the declarers. Thus, the Declaration complies with In re Katz, and removes HIRTENLEHNER or PASTORE as "others" within the meaning of 35 U.S.C. § 102(a).

In order to resolve the difference in inventorship and authorship with regard to Hans GRÖNLUND, Applicants submit herewith

a Declaration under 37 C.F.R. § 1.312 executed by Hans GRÖNLUND stating that he is an inventor of the present application, but was not an co-author of the Vrtala et al. reference because he did not feel that it was necessary for the development of his personal career. It is well known that there are no legal requirements for authorship, and Dr. GRÖNLUND's preference not to be named as an author does not have any legal bearing on inventorship of the present application.

For all of the above reasons, Vrtala et al. is not prior art against the present application. The instant rejection is improper and should be withdrawn.

Vrtala et al. in view of USP '764

The Examiner rejects claims 1-2 and 4-6 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Vrtala et al. in view of U.S. Patent 4,269,764. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

First of all, the subject matter of claim 3 is incorporated into claim 1. As claim 3 is not rejected over Vrtala et al. in view of U.S. Patent 4,269,764, the rejection is overcome.

Applicants respectfully submit that the rejection is moot since Vrtala et al. is not prior art against the present invention.

Withdrawal of the rejection is therefore respectfully requested.

Vrtala et al. in view of USP '764 and '783

The Examiner rejects claims 3 and 21 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Vrtala et al., in view of U.S. Patent 4,269,764, and further in view of U.S. Patent 4,629,783. Claim 3 is canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection applied to the pending claim 21. Reconsideration of the claim and withdrawal of the instant rejection are respectfully requested.

Applicants respectfully submit that the rejection is moot since Vrtala et al. is not prior art against the present invention.

Withdrawal of the rejection is therefore respectfully requested.

Conclusion

As the above-presented amendments and remarks address and overcome the rejections of the Examiner, withdrawal of the rejections and reconsideration and allowance of the claims are

respectfully requested. Should the Examiner have any questions regarding the present application, the Examiner is requested to contact Kristi L. Rupert, PhD (Reg. No. 45,702) in the Washington DC area, at (703) 205-8000.

Pursuant to 37 C.F.R. §§1.17 and 1.136(a), Applicants respectfully petition for a two (2) months extension of time filing a response in connection with the present application and the required fee of $400.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By Kristi L. Rupert #45,702
for Gerald M. Murphy, Jr.
Reg. No. 28,977

P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000

GMM/KLR
Attachments:
Version with markings to show changes made
Declaration under 37 C.F.R. § 1.132 executed by Hans GRÖNLUND

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 3 is canceled.

The claims have been amended as follows:

1. (Twice Amended) An immunogen derived from a protein allergen, comprising:

a) a non-anaphylactic immunogenic recombinant fragment of the protein allergen, said fragment [containing] comprising an IgG epitope and an IgE epitope of the protein allergen partly but not [wholly] completely overlapping [an IgE epitope of the protein allergen];

b) a polymeric form of said fragment, in which form the fragment constitutes the monomeric units, wherein said monomeric units are separated from each other by an oligopeptide linker; or

c) a non-anaphylactic recombinant polymeric form of said protein allergen having 2 to 10 monomeric units in which the protein allergen constitutes the monomeric units, wherein said monomeric units are separated from each other by an oligopeptide linker.